J. Physiol. (1952) 117, 401–414

INHIBITION AND EXCITATION IN SPINAL REFLEX ACTIVITY

By T. GUALTIEROTTI
(Fellow of the Rockefeller Foundation)
From the Physiological Laboratory, University of Cambridge

(*Received* 29 *November* 1951)

Previous work (Martini, Gualtierotti & Marzorati, 1943) has shown that, in mammals, suppression of spontaneous activity in the spinal cord is induced by excitation of a midbrain centre from the cord itself. The locus of this action is situated in the midbrain reticular substance on each side of the mid-line, and the same effect is also produced by direct stimulation of this centre.

Various authors have described inhibitory and excitatory effects on spinal activity following stimulation of higher centres. These centres have been found in several parts of the brain, principally in the reticular formation between cerebellum and diencephalon (Lloyd, 1941), in the anterior cerebellar lobes (Snider, McCulloch & Magoun, 1949), in the midbrain (Gerebtzoff, 1949) and in the medulla oblongata (Magoun, 1950). But it is not yet clear whether there are only inhibitory centres, or only excitatory centres, or both, in the midbrain. Magoun insists that no inhibitory effect can be elicited from higher levels than the medulla, and that every inhibitory action obtained from the midbrain and the diencephalon is due either to damage of the excitatory system or to indirect excitation of the bulbar reticular formation. However, Hess (1931) and Martini *et al.* (1943) obtained chiefly inhibitory effects from the midbrain without any injury. Lloyd (1941) claims that both inhibition and excitation may be produced by stimulating the same area. Lettwin (1948) stimulated the reticular substance between the diencephalon and the medulla, and found that inhibition and excitation were obtained from a single area. The effects could not be due to the cortex because they were still present after its removal. Austin & Jaspar (1950) obtained facilitation of cortically induced and reflex spinal movements from many points of the habenulo-peduncular complex and inhibition from tectum, dorsal hypothalamus and nucleus caudatus.

The present work was planned to obtain further data on the interference of the various parts of the brain (from the diencephalon to the medulla) and of the upper spinal cord in lower spinal activity.

METHOD

Frogs deprived of the telencephalon have been used. The skin-sciatic-gastrocnemius reflex has been used as a test of spinal activity. The reflex was elicited by pressure on the sides of the foot: the results appeared nearly independent of the amount of this pressure, provided it was above a certain value. The pressure was kept constant in any experiment by means of a spring which was extended a fixed amount each time; the pressure itself was maintained for a short time after the end of the reflex response. So each discharge of action potentials began soon after the beginning of the pressure and ended just before its end. Any discharge occurring later is referred to as after-discharge.

Square pulses (1 msec duration, 280/sec frequency: Martini, Gualtierotti & Marzorati, 1943, 1950; Gualtierotti, Martini & Marzorati, 1949) which are effective in stimulating structures of the midbrain when applied to the C.N.S. were applied transversely to excite the spinal cord at cervical or lumbar enlargement level (Fig. 1).

Electrical activity was recorded by means of direct or resistance-capacity coupled amplifiers with a double-beam cathode-ray tube.

The nervous system was sectioned at the following levels (Fig. 1): (I) between telencephalon and diencephalon; (II) between diencephalon and optic lobes; (III) immediately caudal to the optic lobes; (IV) in the lower part of the medulla; (V) in the middle of the cervical enlargement; (VI) at the fourth vertebra immediately under the cervical enlargement, the upper part of the nervous system usually being removed. The section was completed with a rapid single stroke with a razor blade to minimize trauma; whether or not the section was made under anaesthesia did not appear to affect the final result.

Control experiments were carried out under curare or monoiodoacetic acid to eliminate mechanical and muscular artifacts.

Strychnine and nicotine were used either by injection into the dorsal lymph sac or the abdomen, or by direct application to the nervous system.

In some experiments the dorsal tracts of the spinal cord were cut in the middle of the cervical enlargement in order to interrupt some of the afferent pathways to the upper centres.

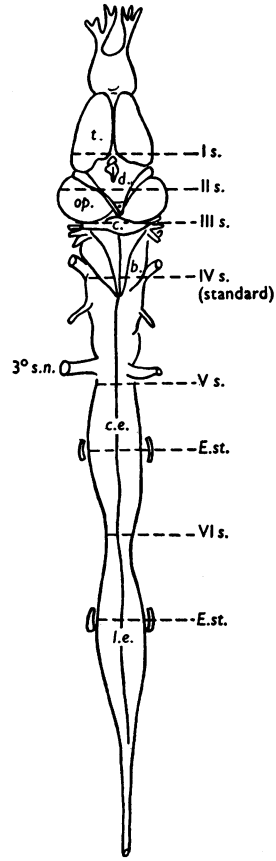

Fig. 1. Diagram of the frog's nervous system. I, II, III, IV, V and VI *s.* sections (see text); *E.st.* points of application of the square current pulses; *t.* telencephalon; *d.* diencephalon; *op.* optic lobes; *b.* bulb; 3° *s.n.* 3rd spinal nerve; *c.e.* cervical enlargement; *l.e.* lumbar enlargement.

RESULTS

Standard reflex (section IV). The reflex in the spinal frog (section IV, Fig. 1) has been taken as the standard with which the reflex in other preparations is compared. In the spinal frog, any injury due to the cut is at a distance from the reflex centre. The reflex is repeatable with only slight variation over long periods in the same frog and differs little in

different animals in its general features, e.g. the duration lies between extreme values of 3–8 sec and is usually about 5 sec (Fig. 2*a*). The discharge is continuous and slowly decreases during the pressure; after the pressure is removed a brief after-discharge may occur, but is often absent.

Reflex activity after various sections

At the beginning of an experiment the mean response of the preparation was determined. It was found to remain constant from 0·5 to 10 hr after cutting, and hence any considerable departure from the mean was assumed

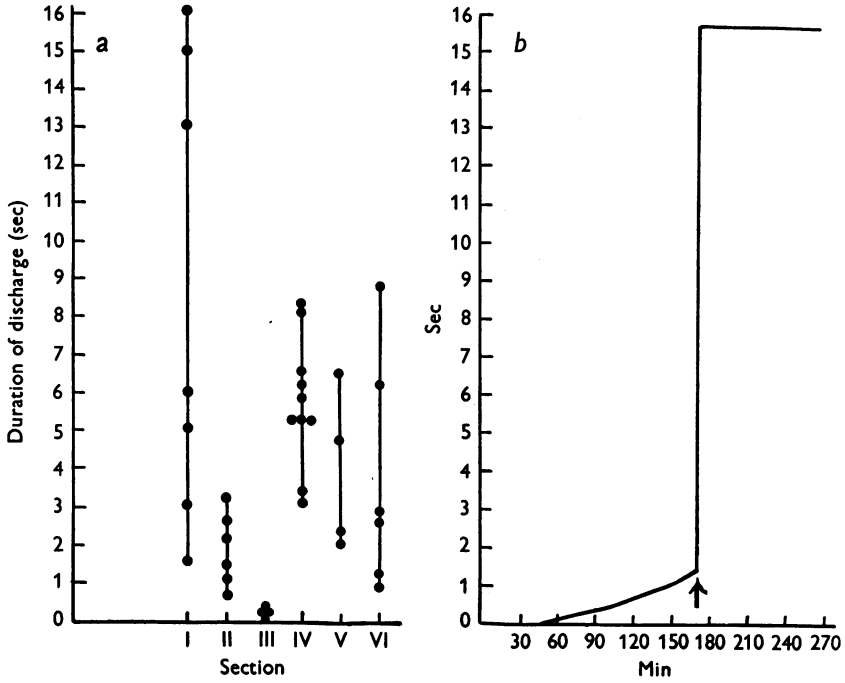

Fig. 2. (*a*) Diagram showing the duration of the discharge after various sections. Ordinate: duration of the discharges in seconds. Abscissa: number of the section. The spots indicate individual experiments. (*b*) Section III. Increasing duration of reflex during the 3 hr following the section. Note the large instantaneous increase in duration (15 sec) after the dorsal tracts are cut (at arrow). Ordinate: duration of the discharge in seconds. Abscissa: time after the section in minutes.

to be due to the experimental procedure. The activity from the ventral roots was recorded to show both spike potentials and non-propagated activity, and in order to control possible artifacts from the escape of muscle action potentials to the electrodes on the nerve.

Section I. When only the telencephalon is removed (Fig. 1) different frogs show wide variations in the duration of the response (Fig. 2*a*). In about 30 % of the experiments the reflex activity is prolonged: mean 13 sec instead of

5–6 sec. In other experiments the activity is similar to the standard reflex; in some the response is much shorter. If the dorsal roots are exposed they must be handled very carefully, as even slight traction may abolish all reflex response for some time. If the motor root is exposed without disturbing the dorsal roots by a lateral exposure, the reflex is present immediately after dissection. When dorsal roots are cut, temporary inhibition of reflex response, or large 'spontaneous' motor discharges may occur. These effects can be avoided by applying novocaine on filter-paper to the cut end; they appear to be due to discharges arising there.

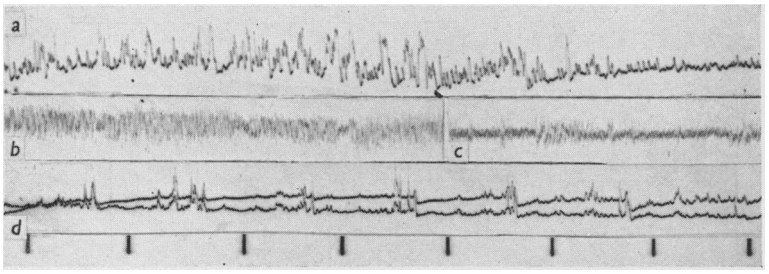

Fig. 3. Records taken (*a*) before, (*b*) immediately after, (*c*) 6 min and (*d*) 1 hr after section through the middle of the optic lobes (section II). All records taken from one ventral root, in *d* recorded with two amplifiers. *b-c* show the spontaneous continuous discharge which lasted 7 min after sectioning the optic lobes. (*a*) and (*d*): reflex response with similar skin stimulation. Time marker: $\frac{1}{15}$ sec.

Section II. With a section between the diencephalon and optic lobes or in the middle of the optic lobes, for the first few minutes there is continuous spontaneous electrical activity in the ventral root and sciatic nerve due to massive impulse discharges. This shortly subsides and then there is no response to stimulation for about half an hour. Later, spontaneous and reflex activity reappears: it is limited in number of units and in duration (Figs. 2*a*, 3).

Section III. In the section between the optic lobes and the medulla (some damage to the cerebellum and midbrain is unavoidable, but most of the midbrain and the medulla are intact) there is an initial big discharge as described for section at level II; afterwards the normal reflex activity is very brief (Fig. 2 *a*); often a big after-discharge occurs. After about 2 hr the reflex response increases in duration, and if the dorsal tracts are now cut, the response becomes very long (16 sec) and remains thus during the rest of the experiment, while the after-discharge decreases (Fig. 2*b*).

Section IV. Section IV gives the response taken as standard (see above).

Section V. With section at level V the normal activity is similar to that in the spinal frog, but occurs in fewer motor units. When this section is limited to the posterior tracts, the reflex activity is identical with that in the spinal frog (section IV, Fig. 2*a*).

Section VI. Removal of the cervical enlargement and upper nervous system (Fig. 1) has little direct effect on the reflex. The only change is that the duration immediately becomes equal to the standard duration.

Effect of strychnine

Section I. The effect of strychnine has two phases. At first, reflex activity is increased, but the discharge is not synchronized in many motor units (Fig. 4). Later a characteristic synchronization develops as in the spinal frog (Fig. 6). Sometimes, a transitional phase of sinusoidal activity is observed (Fig. 4 *d*).

Section II. Strychnine has the same effect as in section I (Fig. 5). By applying strychnine on the cervical enlargement only the second phase is evident.

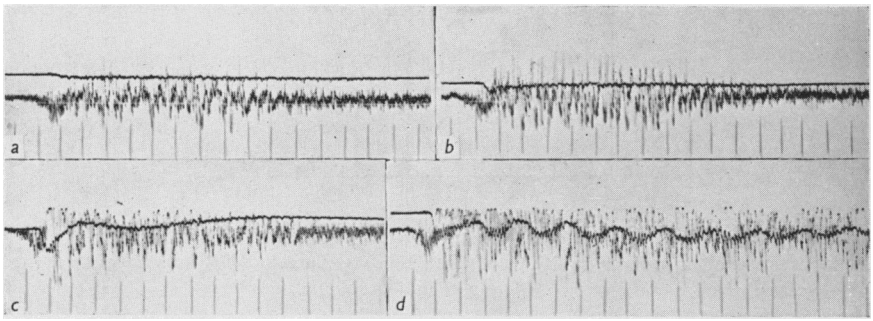

Fig. 4. Section I. The effect of strychnine: (*a*) normal reflex response; (*b*) 4 min after injection; (*c*) 6 min after injection; (*d*) 7 min later. Upper record: ventral root. Lower record: sciatic nerve. Time marker: $\frac{1}{15}$ sec.

Section III. Strychnine has the same effect as section I above.

Section IV (*standard*). Subconvulsant doses of strychnine may double the amplitude and halve the frequency of potentials recorded from a needle electrode in gastrocnemius (Fig. 6). This appears to be due to increasing synchronization of the motoneurones. This synchronization is also evident in the first stage of convulsant doses, after which group activity appears. The strychnine response begins abruptly with the sinusoidal waves previously described. The strychnine group discharges last almost without interruption till the preparation is exhausted. Often the synchronization is complete: a single synchronous wave takes the place of the groups of spikes (Fig. 6 *d*); that this is due to synchronization of a number of units is suggested by the initial incomplete fusion of the potentials and the gradual decrease in amplitude as this discharge continues (Fig. 6 *d*).

Section V. After strychnine, if only the posterior tracts are cut, at first the reflex is prolonged and not synchronized: in one experiment this was seen for 22 min before the synchronous groups appeared. With complete section, when

the upper part of the nervous system is removed, the first phase is completely absent and the second is much reduced. This is illustrated in Fig. 7*b*, where the only effect of strychnine is the transitory appearance of small groups of

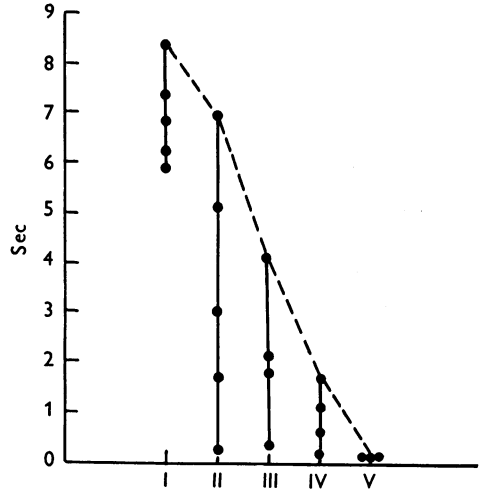

Fig. 5. Diagram showing the duration of the massive reflex discharges after strychnine. Section IV in this case includes about half the medulla. Ordinate: duration of the discharges in seconds. Abscissa: number of the section. The spots indicate single experiments.

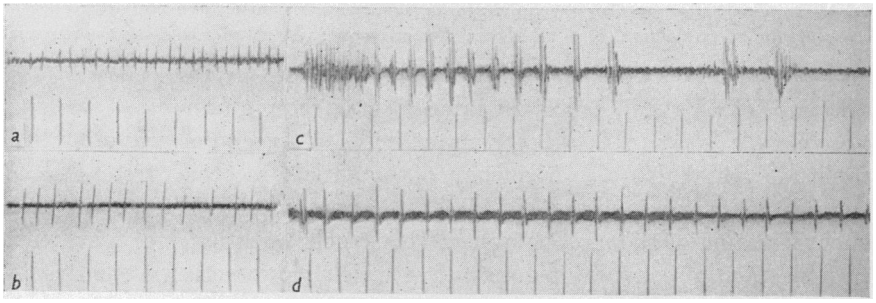

Fig. 6. Section IV (standard). Records from a needle electrode in the gastrocnemius muscle during standard reflex stimulation. (*a*) normal; (*b*) after subconvulsant doses of strychnine; (*c*) 3 min after convulsant doses of strychnine; (*d*) 6 min after convulsant doses of strychnine. In (*b*) the frequency becomes about one half that in (*a*) and the amplitude approximately doubles. In (*d*) a very strong synchronizing effect reduces the small groups of spikes in (*c*) to a volley of single waves of decreasing amplitude. Time marker: $\frac{1}{15}$ sec.

low amplitude potentials. After a short time the normal reflex activity decreases slowly till it disappears. If, after section, the upper part of the cervical enlargement is left in contact with the lower, the group effect does not

always disappear completely, but the intervals between the groups are prolonged and the number of potentials in each group is increased.

Section VI. There is no potentiating effect of strychnine on the reflex whether it is given by injection into the abdomen or by direct application to the lumbar enlargement; on the contrary, the reflex activity gradually decreases to nothing (Fig. 8). If a cut at level VI is made soon after group synchronization has appeared, normal reflex activity appears again for some

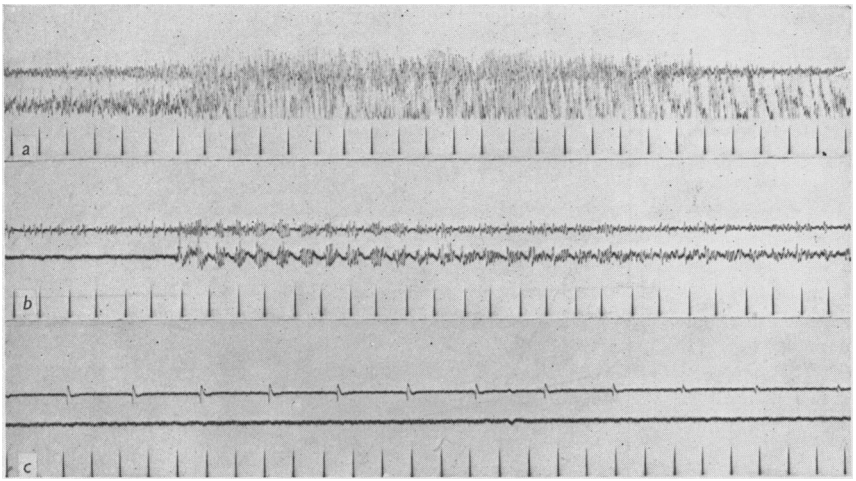

Fig. 7. Upper record: gastrocnemius muscle. Lower record: sciatic nerve. (*a*) section I. Spontaneous discharge 20 sec after the injection of nicotine into the abdomen. (*b*) section V. 5 min after strychnine; strychnine bursts are seen only in the middle of a normal reflex response. After the beginning of the strychnine effect, potentials of much greater amplitude may be seen; the activity of the nerve suddenly becomes visible, although the gain was such that the normal potentials could not be recorded. (*c*) section III. A single wave discharge decreasing in amplitude after lasting 8 sec follows direct stimulation of spinal cord (see text). Time marker: $\frac{1}{15}$ sec.

minutes. But a cut made later does not restore normal reflex activity. In the untreated spinal frog a cut at level VI has little effect. In all these preparations, when the upper part of the nervous system is not removed, the muscles of the frog in the area connected with the part of the spinal cord above the cut show typical strychnine convulsions.

Effects of nicotine

Section I. Twenty seconds after nicotine has been injected into the abdomen, big spontaneous discharges appear and continue for 20 min with short interruptions and then gradually disappear during the next 10 min (Fig. 7*a*). The reflex activity can only be tested between the bouts of spontaneous activity which it then resembles.

Section III. Nicotine has the same effect as in section I. If, in addition, the dorsal tracts are cut the nicotine effect is altered. The spontaneous discharges become shorter with more frequent intervals. It was impossible to test reflex activity in these conditions.

Section IV (*standard*). Nicotine has no excitatory effect in the spinal frog, but abolishes reflex activity in about 4 min (Fig. 8). If used in conjunction with strychnine, nicotine increases the frequency of groups; at the same time the number of spike potentials in each group is reduced.

Section VI. Nicotine abolishes the reflex activity as in the spinal frog (Fig. 8).

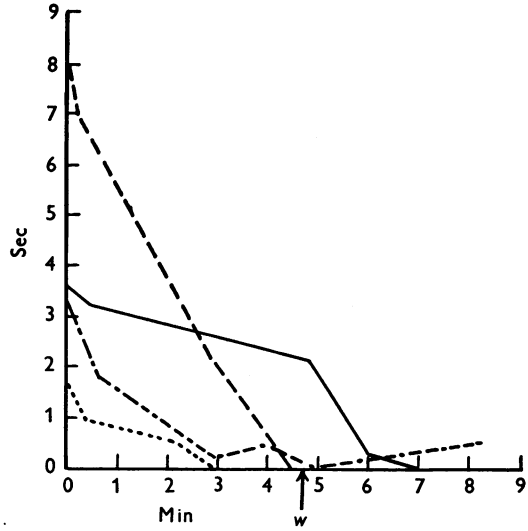

Fig. 8. Diagram showing exhaustion of reflex activity after nicotine and strychnine. Ordinate: duration of discharge in seconds. Abscissa: time in minutes after injection of the drugs or their application to the lumbar enlargement. - - - - -, section IV after nicotine injection; ———, section VI after strychnine injection; ·—·—·—, section VI after strychnine application to the lumbar enlargement. At *w* it is washed off; ....., section VI after nicotine injection.

Effects of electrical stimulation of central structures

Section I. During stimulation (square pulses, 15 V at 280/sec for 5 sec) applied on the external sides of the second vertebra, a massive discharge of impulses is seen in the ventral root followed by an after-discharge of about 0·5–1 sec; and then for about 10 min no reflex response can be obtained. The response slowly returns to normal and sometimes is enhanced. The reflex is not inhibited by central stimulation if (*a*) the posterior tracts are cut above (but not below) the level of the stimulus; (*b*) the strength of stimulus is reduced, although a discharge still occurs during stimulation and is followed by prolonged firing of many units; (*c*) the preparation has been kept for many hours: the suppression of the reflex does not occur although the reflex itself is still normal;

(*d*) repeated injuries are produced by dissection, especially of the posterior roots; (*e*) the adequate stimulus is only applied for about 0·5 sec: only the immediate excitatory effect is seen. After strychnine the reflex is only momentarily inhibited by central stimulation. Spontaneous activity is suppressed (Fig. 9 *a*, *b*), but 15 sec later one or two groups of spikes are elicited by the reflex stimulation, and after 1 min the strychnine activity is completely restored (Fig. 9 *b*).

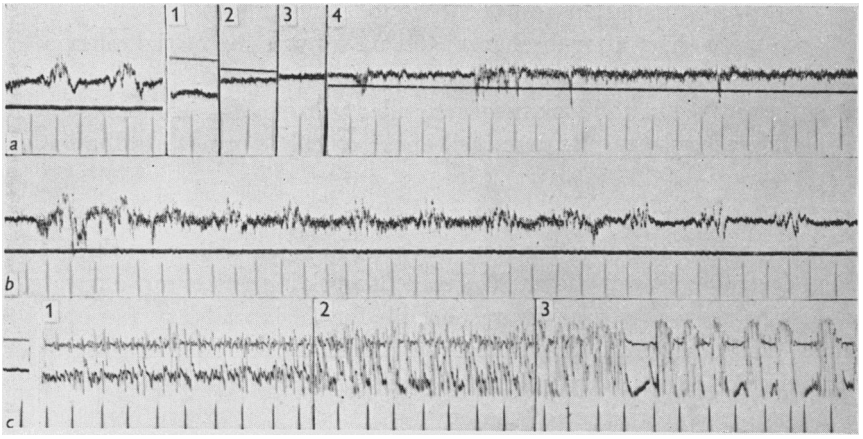

Fig. 9. Section I. The prolonged spontaneous strychnine discharge is suppressed by square pulse stimulation. (*a*) spontaneous strychnine bursts before stimulation, *a* 1: immediately after stimulation. During *a* 1–2–3 interruption of the spontaneous discharges occurs: a slow potential in the motor root which appeared during the stimulation progressively decreases to nothing. *a* 4: reflex stimulation elicits a reduced response. Intervals between *a* 1, 2, 3 and 4 are $\frac{1}{2}$ sec each. The suppression lasts about 1 min. (*b*) reflex response 1 min later; the reflex stimulation elicits strychnine bursts which continue spontaneously after the end of stimulation. (*c* 1–2–3) the same experiment in the same preparation after cutting the dorsal tracts in the upper third of the cervical enlargement about 2 mm above the point of application of the electric stimuli. Interval between *c* 1 and 2 is 3 sec; between *c* 2 and 3 is 2 sec. Note the lack of suppression and the big discharges which follow the stimulation. Upper record: nerve (except in *a* 1 and 2). Lower record: ventral root at very low gain. At *c* 1–2–3 the gain is increased to show the fast activity. Time marker: $\frac{1}{15}$ sec.

If the stimulus is weakened the reflex response is not suppressed but is reduced to three or four groups of spikes which are further apart and involve fewer motor units.

Section II. It differs little from section I above, but the suppression of the reflex is not so long.

Sections III–IV. When the cephalic end of the medulla is damaged, stimulation does not suppress the reflex, but it elicits a series of synchronized discharges which lasts for several seconds (Fig. 7*c*). The potentials are of longer duration than normal, occur with almost constant frequency, and gradually decrease in amplitude. The reflex response was first tested 3 sec after the

square pulses; it was then normal. When the section is made further back in the medulla, stimulation was found not to suppress the reflex.

Section V. With complete section, and removal of the upper part, stimulation results in a very short after-discharge and there is no suppression of the reflex even immediately after stimulation. When only the posterior tracts are cut there is the same absence of suppression; but the immediate response to the stimulus is prolonged and increased.

Section VI. Stimulation across the lumbar enlargement produces a large discharge, with short after-discharge, and no suppression of the reflex at all: 2 sec after the current a normal reflex response is obtained.

If curare sufficient to block neuromuscular transmission or monoiodoacetic acid be injected, the results described above are little or not at all altered.

DISCUSSION

The great variability of reflex response seen in frogs with only the telencephalon destroyed is well known. The present work is an attempt to trace what parts of the nervous system are responsible for this variability and how they may be activated from lower parts of the C.N.S. or from the periphery. A reflex which is relatively inflexible in the spinal animal is greatly modified by the presence or absence of the brain stem, and it is shown here that this modification can be altered by impulses arising from stimulation of the spinal cord itself and also (reported separately) by impulses from the periphery, all these effects being abolished by cutting the spinal tracts: from which it is concluded that ascending impulses are responsible. The upper centres can cause facilitation or inhibition of the spinal reflex; this does not appear to be determined by the locus but by the intensity of the effects produced by stimulating the spinal cord.

Previous work on mammals seems to show similar effects which various authors (Lloyd, 1941; Martini *et al.* 1943; Gerebtzoff, 1949; Magoun, 1950) have ascribed to the reticular formation: some have suggested that its function is to control the nervous system with special centres for each part of it. Whether the effects are excitatory (as Magoun, McCulloch, Moruzzi, etc., claim) or inhibitory (according to Hess, Martini, Gualtierotti & Marzorati, etc). has been a matter of dispute. The present results suggest, if analogy with the frog holds good, that those who found only excitation were not using a strong enough stimulus. In addition, as shown above, fatigue and injury are particularly likely to destroy inhibitory effects. Magoun himself found an inhibitory effect, together with an excitatory one from the medulla and from the cerebellum. But at higher levels of the midbrain and diencephalon he found no inhibition with direct stimulation; this may be due to a high threshold of the reticular formation towards the cephalic end, or it may be that the current spread has rendered the stimulus less effective in these deep

structures where it is difficult to ensure localization of the stimulus; and earthing of the animal is necessary to avoid stimulation via the capacity of animal and stimulator to earth. These difficulties disappear when the inhibitory effect is obtained by reflex stimulation or by excitation of the appropriate afferent pathways: this can be done via the spinal cord (Martini *et al.* 1943). Magoun found that a very strong stimulus had to be used to obtain spinal inhibition on exciting the cerebellum locally; with square pulses (300/sec) he found no effect unless 15–45 V was applied to the electrodes. This may explain the negative results on the cerebellum lately obtained by Arduini, Moruzzi & Terzuolo (1951), who used less than 6 V. That a strong repeated stimulus is necessary to cause inhibition is also shown by the observation that cutting the dorsal tracts with a single knife cut does not provoke inhibition, although it must stimulate all the fibres cut; after the cut not only is the square current no longer effective, but the reflex response increases, which may be due to cutting off inhibitory impulses previously ascending from the spinal cord.

In conclusion, there appears to be quite a definite system of communication between centres in the brain and spinal cord, and this functions as a unit. In this way there is control over spinal activity by these centres in the brain, in the form of either excitation or inhibition according to circumstances (see diagram in Fig. 10). The efferent pathways of the inhibitory and excitatory stimuli appear to be situated in the ventral spinal cord, because these effects are still present when the dorsal tracts are severed below the stimulating electrodes. The afferent pathways appear to be the dorsal tracts and the dorsal roots, because if these are severed rostral to the point where the spinal cord is directly stimulated there is no further inhibition or facilitation. The factor which determines whether inhibition or excitation will occur is the strength of the stimulus, for a relatively weak stimulus causes excitation while a stronger stimulus causes inhibition. The same reflex centre in the spinal cord to which sensory impulses go from the periphery sends further impulses to the brain centres and in turn receives from them either facilitation or inhibition.

During the present experiments the phenomena of facilitation or depression of the particular response were observed throughout. This could happen spontaneously with the more or less normal inflow of sensory stimuli, or during and after injuries of different degrees, e.g. traction on the dorsal root.

The conditioning centres in the brain appear to be situated somewhere between the rostral limit of the diencephalon and the rostral limit of the medulla. It is difficult to ascertain their exact situation in frogs because the difference (mainly in duration) between the effects obtained by cutting at various levels might be ascribed not to the presence or removal of some essential areas, but to a far-reaching influence of the cutting itself. However, the same functional unit described above, relating to the spinal pathways, is

involved also in the inhibitory effects of sections through the optic lobes. This is proved by the fact that these effects disappear when the dorsal tracts are severed. In diencephalic preparations the direct action of the cut on the centres in question seems less likely. This is indicated by the more intense and prolonged inhibition or facilitation respectively after peripheral stimulation. The great variability of reflex response from one preparation to another, while the reflex activity maintains the same character in each one, appears to be due to peripheral injuries or to the rate of the normal inflow, i.e. to local

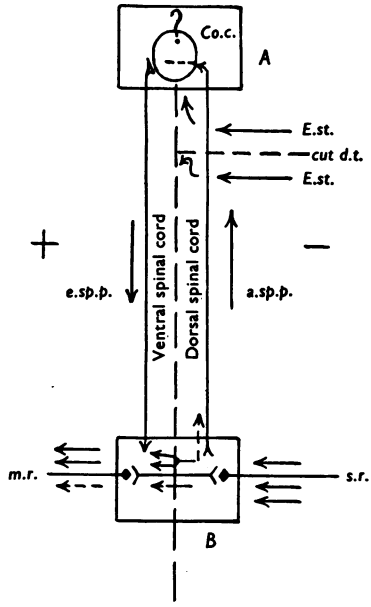

Fig. 10. Schematic diagram of the inhibitory-excitatory mechanism between the spinal cord and the brain. *A*: diencephalon-midbrain area. *Co.c.* supposed controlling centre. *B*: spinal reflex arc. *E.st.* loci of electrical pulse stimulation; *cut d.t.* section of dorsal tracts; *e.sp.p.* efferent spinal pathways; *a.sp.p.* afferent pathways of the brain controlling centre; *s.r.* sensory root; *m.r.* motor root. The doubling of arrows means increased strength of stimulation or bigger reflex discharges. Dotted arrows mean decreased reflex response.

peripheral conditions. For instance, traction on, or damage to, a dorsal root causes the preparation to pass into a state of continuous inhibition which is more or less complete. This inhibition disappears when the spinal cord as a whole or only the dorsal tracts are severed.

The action of the brain centres in causing inhibition or stimulation in the spinal cord is related to changes of the potential level of the spinal cord; this will be described in a separate paper. In conclusion, it may be said that the mechanism described above appears to be another example of autoregulation analogous to what occurs when muscular contraction is controlled by sensory impulses from the muscles themselves through the spinal centres.

Bremer's findings on the activity of the spinal cord after strychnine are confirmed: if a cut is made across the middle of the spinal cord the interval between the bursts of reflex activity becomes very prolonged, but if the upper part is removed then the whole strychnine effect disappears. In this case, if no more than 9–15 min have elapsed, the reflex response becomes similar to that before strychnine. Thus, as Bremer (1950) showed, there seems to be a mutual interaction between two parts of the spinal cord which have just been divided and are still remaining in close contact. If more than 15 min elapse from the strychnine injection, then removal of the cervical enlargement stops the strychnine effect, but no more reflex activity can be elicited. In the lumbar preparations strychnine not only fails to excite, but on the contrary destroys reflex activity gradually in about 10–15 min; if strychnine is not injected but applied directly to the lumbar enlargement the same result is obtained. Hence it appears that strychnine is effective only on particular zones. Many examples of this exist. Strychnine is not active on the cerebellar cortex (Dow, 1938), but it can induce there discharges of lower frequency and higher amplitude than normal when applied to the pons-bulbar formations (Gualtierotti & Capraro, 1941).

The depressing action of strychnine and nicotine on the activity of lumbar preparations seems to be due to an induced local blocking of neurones, but this is overcome when a large number of them are connected together, especially when firing synchronously. Spinal frogs, in fact, show a considerable reflex and spontaneous activity after strychnine (synchronous discharges) and the intact frog does so after nicotine (asynchronous activity). The reflex response and the spontaneous discharges last much longer than the time necessary to depress completely the responses in lumbar preparations; however, it can be proved that the block on neurones exists in this case also by severing the cervical enlargement (or only the brain centres if nicotine has been injected). Depression of reflex activity is then observed.

SUMMARY

1. The spinal reflex activity of the frog, elicited by pressure applied to the foot, has been recorded from a ventral root, sciatic nerve and gastrocnemius muscle after sections in the brain stem and in the spinal cord. The reflex response in the spinal frog has been chosen as the standard with which the other preparations are compared. No big difference exists between the standard and the other spinal sections. The diencephalic preparation shows much more variable reflex activity. Following brain stem sections in the region of the optic lobes there is a prolonged discharge and later the reflex response is brief.

2. The action of strychnine under these conditions has been investigated. In diencephalic-bulbar frogs a massive reflex response occurs, but this is no

longer present in spinal frogs. When the upper part of the cord is removed the reflex activity gradually disappears. Nicotine produces a prolonged spontaneous discharge, which is absent in the spinal frog.

3. With diencephalic frogs strong electrical stimulation of the cervical enlargement induces a prolonged inhibition, but this is absent in spinal frogs. The inhibition lasts for several minutes after the end of the stimulation and can be stopped by cutting the spinal cord or the dorsal tracts above the level of the stimulus. Weaker electrical stimulation can cause facilitation: thus a stronger stimulus is needed to inhibit than to excite. These effects appear to result from stimulation of centres in the brain.

4. No evidence has been found to suggest that the inhibition and excitation arise in different regions of the brain stem; the difference between them seems to be correlated only with the strength of stimulation. These results are discussed with reference to the findings of other authors.

The author wishes to thank Prof. E. D. Adrian for the hospitality of his laboratory; Dr B. H. C. Matthews for his supervision and assistance during the work; the Rockefeller Foundation for a personal grant; and the Medical Research Council for apparatus.

REFERENCES

Arduini, A., Moruzzi, G. & Terzuolo, C. (1951). *Arch. Fisiol.* **50**, 328.
Austin, G. & Jaspar, H. (1950). *Fed. Proc.* **9**, 6.
Bremer, F. (1950). *Abstr. XVIII int. physiol. Congr.* p. 12.
Dow, R. S. (1938). *C.R. Soc. Biol., Paris*, **128**, 38.
Gerebtzoff, M. A. (1949). *Arch. int. Physiol.* **56**, 286.
Gualtierotti, T. & Capraro, V. (1941). *Arch. Sci. biol.* **27**, 247.
Gualtierotti, T., Martini, E. & Marzorati, A. (1949). *J. Neurophysiol.* **12**, 363.
Hess, W. R. (1931). *C.R. Soc. Biol., Paris*, **107**, 333.
Lettwin, J. Y. (1948). *Fed. Proc.* **7**, 71.
Lloyd, D. P. C. (1941). *J. Neurophysiol.* **4**, 115.
Magoun, H. W. (1950). *Physiol. Rev.* **30**, 1459.
Martini, E., Gualtierotti, T. & Marzorati, A. (1943). *Pflüg. Arch. ges. Physiol.* **246**, 585.
Martini, E., Gualtierotti, T. & Marzorati, A. (1950). *J. Neurophysiol.* **13**, 1, 5, 113, 117.
Snider, R. S., McCulloch, W. S. & Magoun, H. W. (1949). *J. Neurophysiol.* **12**, 325.